Docket No. 45858/55672

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: Goldsborough, et al. EXAMINER: B. Sisson

SERIAL NO. 09/725,897 GROUP ART UNIT: 1634

FILED: November 30, 2000

FOR: METHODS FOR THE STORAGE AND SYNTHESIS OF NUCLEIC ACIDS USING A SOLID SUPPORT

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By Sharon Bizokas

Sir:

DECLARATION OF DR. NAVIN PATHIRANA PURSUANT TO 37 CFR 1.132

I, Dr. Navin Pathirana, declare as follows:

1. I am presently a Senior Scientist at Whatman, Inc., the United States subsidiary of Whatman plc, United Kingdom. I have been employed in this position since April 2002. I am an experienced Ph.D. scientist with over ten years of chemical and biochemical research and development experience, particularly in the development of products and methods for chromatographic and diagnostic applications, surface modification methods, proteomics, and nucleic acid separation and isolation. Prior to my current position at Whatman, I had

previously been employed in a variety of positions with Whatman plc and its subsidiaries. From 2000-2002, I was a Principal Scientist with Whatman BioScience Ltd. in Cambridge, U.K., where I developed new formats for DNA isolation and purification columns and systems and oversaw developments in proteomics and Microsystems. From 1996-2000, I was a Senior Research Technologist with Whatman International Ltd. in Kent, U.K., where I developed new products and technologies for protein purification and immunodiagnostics. Prior to that I was a Senior Technologist (1993-1996) and a Development Chemist (1990-1993) with Whatman International Ltd. in Kent, U.K. I have been listed as an inventor on several patent applications. I hold a B.Sc. (Hon) in Chemistry with First Class Honors from the University of North London, London, U.K. I also hold a Ph.D. from the University of North London, London, U.K., where I served as a Research Fellow (1987-1990). My thesis was entitled, "Chemistry and Biological Activity of Iron Quinoneoximic Compounds," and I studied the synthesis and properties of chelators for the treatment of iron over-load. In addition, I have a Professional Certificate in Management from The Open University, U.K., and a Certificate in Project Management from the University of New England, Maine.

2. The subject application discloses among other things and claims a method of producing one or more cDNA molecules comprising (a) contacting a sample comprising a cell or a virus with a solid medium, wherein (i) the sample comprises mRNA and genomic DNA; (ii) the mRNA comprises an mRNA template of interest; and (iii) wherein the solid medium comprises a matrix; and a composition for inhibiting degradation of the mRNA template, wherein the composition comprises a detergent or surfactant; and the composition is sorbed to the matrix then dried prior to contact with the sample; (b) sorbing at least a portion of the mRNA template to the solid medium; (c) eluting the mRNA from the solid medium while retaining the genomic DNA; and (d) contacting the mRNA with one or more reverse transcriptases under conditions sufficient to synthesize one or more cDNA molecules complementary to all or a portion of the mRNA template of interest.

3. Traditionally, a sample containing nucleic acid (including, but not limited to, a biological sample, such as a cell sample) has been used for isolation of nucleic acid. Cells in the sample have been lysed, and the nucleic acid extracted, optionally washed, and isolated. The method typically required a series of steps applying various reagents, engaging in one or more centrifugation steps, and transferring materials between test tubes, microfuge tubes, or microwell plates. The isolation method typically required precipitation with alcohol at a low temperature (e.g., at, or more often below, 0°C; usually between -20°C and -70°C). The nucleic acid would then be subjected to various types of analyses. For some experiments, such as reverse transcription or Northern blotting, the isolation of ribonucleic acid (RNA), particularly messenger RNA (mRNA), is desired. In addition, the researcher may also find it necessary or desirable to separate the RNA from other nucleic acids, such as deoxyribonucleic acid (DNA). RNA is typically single stranded, is generally less stable than DNA, and is subject to breakdown by ribonucleases (RNAses), which are enzymes that degrade RNA and which contaminate many surfaces and solutions. As a result, techniques for isolating DNA needed to be modified for use in RNA isolation. In general, RNA research required extra precautions and treatments and the use of dedicated materials and equipment.

4. The current invention addresses these concerns and many other issues as well, such as protection from contamination by reducing the materials used and the number of experimental steps.

5. I have reviewed the Patent Office Action ("2004 Office Action") dated August 13, 2004, and the Patent Office Action ("2002 Office Action") dated March 26, 2002, issued in connection with the subject application. As I understand the Office Action, the Patent Examiner has objected to the specification as having incorporated essential matter by reference, such as protocols for synthesizing complementary deoxyribonucleic acid (cDNA) from isolated messenger ribonucleic acid (mRNA).

6. I disagree with this objection.

7. The current invention illustrates that it is possible to separate RNA from genomic DNA, in order to produce complementary DNA (cDNA), by contacting a cell or a virus with a solid medium comprising a solid matrix and a composition for inhibiting degradation of the mRNA template, wherein the composition comprises a detergent or surfactant sorbed to the matrix then dried prior to contact with the sample, subsequently followed by eluting the mRNA while retaining the genomic DNA, and then by contacting the mRNA with one or more reverse transcriptases under conditions sufficient to synthesize one or more cDNA molecules complementary to all or a portion of the mRNA template of interest. The specification of the current patent application provides, among other things, examples of this type of isolation and cDNA synthesis.

8. In one aspect of the invention, the mRNA is isolated from genomic DNA in a sample using the solid medium described above, and then the mRNA is used as a template for cDNA synthesis. One such example is provided at page 28, lines 1-20, of the application as filed. Other examples are provided, e.g., at page 29, lines 19-27, and at page 31, lines 13-22, of the application as originally filed. Additional examples are provided throughout the Examples from page 24, line 25, to page 32, line 5, and elsewhere in the specification as originally filed.

9. Alternative protocols for reverse transcribing previously isolated mRNA to produce cDNA had been known in the art at the time when the application was filed. One example can be found in Sambrook et al., Molecular Cloning: A Laboratory Manual (2^{nd} ed.), Cold Spring Harbor Laboratory Press, pp. 8.60-8.65 (1989). These pages outline protocols for first and second strand cDNA synthesis starting with previously isolated poly(A)$^+$ RNA. Most mature mRNA molecules have a poly(A) tail, which can be used either to isolate poly(A)$^+$ RNA and/or to reverse transcribe it with a reverse transcription primer having an oligo(dT) sequence (oligo(dT) primer). The protocols described on these pages of this

laboratory manual are examples known to those of skill in the art at the time when the present application was filed.

10. I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 13th July 2005

Navin Pathirana, Ph.D.